Exhibit 10

August 3, 2020

EXPERT REPORT OF JUDITH FEINBERG, MD

In re National Prescription Opiate Litigation

I. INTRODUCTORY STATEMENT – OVERVIEW

The opioid epidemic is now one of the greatest public health problems that the United States (U.S.) faces. Opioid overdose deaths rates have increased steadily for over a decade and doubled from 2013-17 as the highly potent synthetic opioid fentanyl entered the drug supply (NIDA 2020). In 2017, there were over 70,237 drug-related deaths, more than were observed in the U.S. at the height of the AIDS epidemic, and a 9.6% increase over 2016 (NIDA 2020). After a small decrease in 2018 (Hedegaard), overdose deaths in 2019 rose 4.6% in 2019 to 70,980, including 50,042 involving opioids, according to preliminary CDC data (CDC July 16, 2020). The surge in drug-related deaths over the past several years largely accounts for the decrease of U.S. life expectancy to 78.6 years in 2017, down from 78.7 years in 2016 and 78.9 years in 2014 (Arias 2019). Evidence points to prescription opioids as an "on-ramp" to the development of opioid use disorder (OUD) with most opioid-related deaths prior to 2010 due to prescription opioids (Jalal 2018- see figure). Investigators have the trajectory of current opioid misuse as initiation with prescription opioids, and as these pills became harder to obtain and more expensive and as heroin of increased purity became available at a fraction of its previous cost, transitioning to smoking or snorting heroin and eventually to injection despite fear and stigma of injection drug use (IDU)(Mars 2014, Botticelli 2016).

The City of Huntington and Cabell County have been particularly hard-hit by the opioid epidemic. According to health summary statistics for Cabell County, "A significant increase in heroin use, property crimes, 911 calls, and deaths due to overdose have been well documented… Overdose rates are far greater than rates reported in other cities across the country" (CHHD 2015, p. 4-see figure). New data in 2015 demonstrated that "…there has been a substantial increase in drug offenses geographically from 2005 to 2014, …grams of heroin seized from 2010-2013, and…increase in 911 overdose calls. Most astounding is the rate at which heroin overdose deaths are occurring and the estimated medical costs of substance abuse in Huntington and Cabell County." (CHHD 2015, p. 49- see figures).

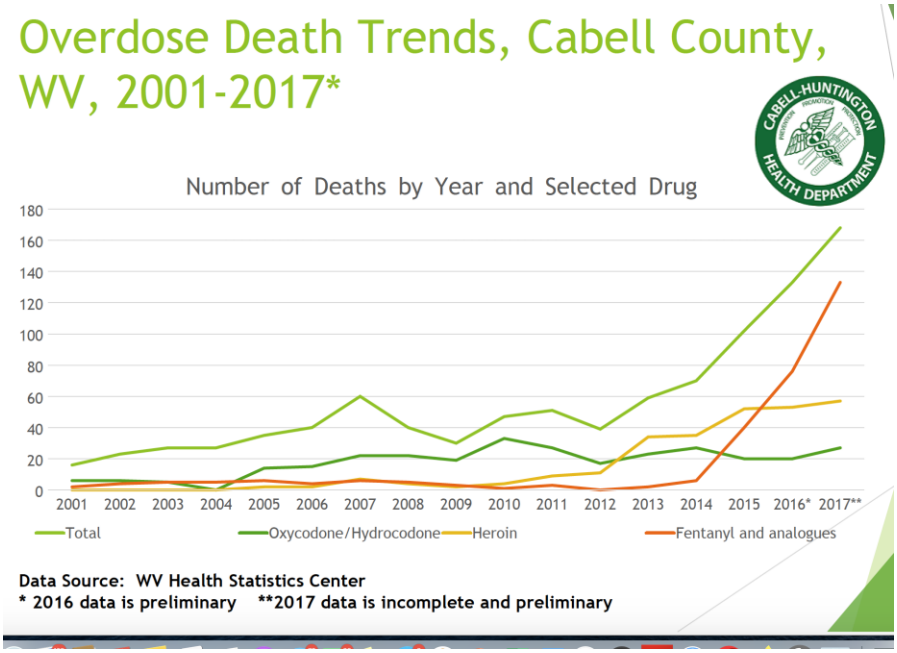
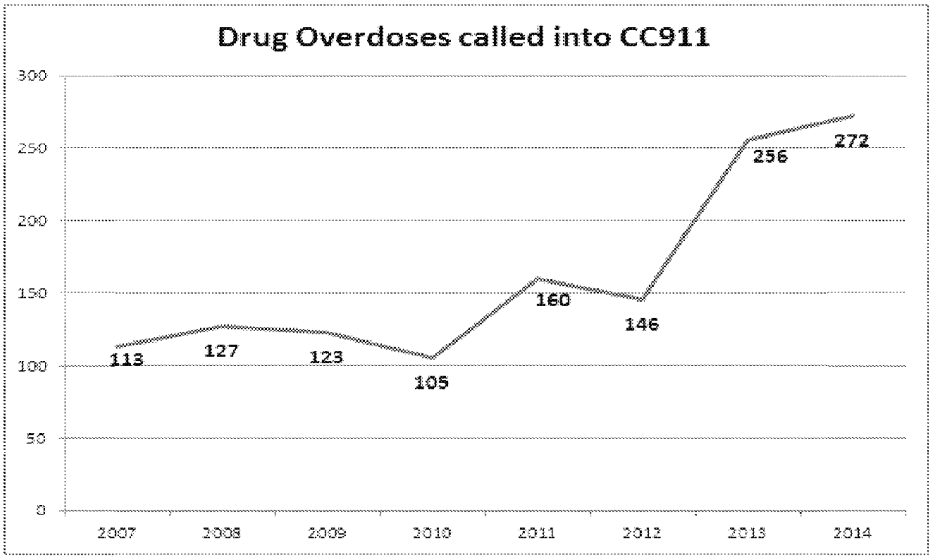


Figure 84. Drug overdose 911 calls, Cabell County, 2007-2014.



Source: Huntington Mayor's Office on Drug Control Policy, 2015

CHHD 2015, p. 50

In 2016, the Cabell Huntington Health Department (CHHD) conducted a survey of 1,899 clients of its syringe services program to evaluate the age at first drug use and drugs of choice. That year, the first full year of the CHHD syringe services program, the program served 1,980 people who inject drugs, of whom 56% were male, 20% homeless and 34% uninsured (M. Kilkenny MD). Almost all (99.7%) responded to the survey. The average age of first drug use—prior to initiating injection---was 17.8 years old (range, 2-65 years). Regarding drugs of choice, the vast majority (91.3%) reported heroin, with other opioids (19.3%) and Suboxone (11.1%) also used; smaller proportions preferred the stimulants methamphetamine (19.6%) and cocaine (15.7)(CHHD Physician Director M. Kilkenny MD).

Opioid overdoses are not the only life-threatening consequence of the drug epidemic—the serious infections associated with drug use and especially injection opioid use have resulted in a series of syndemics, intertwined epidemics that are part of the complex public health crisis we are currently facing that will be described in detail below.

II. BACKGROUND AND QUALIFICATIONS

a. **Education, Residencies, and Fellowships**. My name is Judith Feinberg. I am an internist and specialist in Infectious Diseases at the West Virginia University School of Medicine. I am both a tenured Professor of Behavioral Medicine and Psychiatry and tenured Professor of Medicine/Infectious Diseases; in August 2019 I was named the first E.B. Flink Vice Chair of Medicine for Research. My activities include: research- 50%, research administration and faculty mentoring- 35%, and teaching- 15%. Although I have active licenses to practice medicine and hospital privileges in both West Virginia and Ohio, at the current time I am not seeing patients. In 2014, I developed Ohio's third

syringe exchange and its first full syringe services program, the Cincinnati Exchange Project, after 9 years of effort.

I have been retained by Counsel for Plaintiffs Cabell County and City of Huntington to provide my scientific expertise regarding the impact of the opioid epidemic on infectious diseases among people who use drugs, nationally and in the City of Huntington and Cabell County, West Virginia, and ways to abate or reduce the harms caused by these infections. My current research focuses on the recognition, diagnosis, treatment and prevention of drug use-associated infections, especially those acquired through injection drug use (IDU), such as HIV, hepatitis B and C, and endocarditis. My previous research focused on the management of HIV/AIDS for several decades.

b. **Certifications**. I received my undergraduate degree from the University of Chicago in 1967 and my medical degree from Rush Medical College of Rush University in Chicago in 1979. I completed internship and residency in internal medicine at Rush-Presbyterian-St. Luke's Medical Center in Chicago and a fellowship in infectious diseases at the University of California, Los Angeles. I am a diplomate of the American Board of Internal Medicine (ABIM) and a diplomate of the ABIM Subspecialty Board in Infectious Diseases. I am currently licensed to practice medicine in West Virginia and Ohio.

c. **Hospital Appointments**. Past: Johns Hopkins Hospital, Baltimore (1990-1995), and University Hospital, Cincinnati (1995-2015). Since December 2015, I have been employed by West Virginia University School of Medicine; its affiliated hospital is J.W. Ruby Hospital, Morgantown. I am also affiliated with The Christ Hospital, Cincinnati, and its Lindner Research Center since 2017.

d. **Professional Appointments**.

i. Current (since 2015): West Virginia University School of Medicine Professor of Behavioral Medicine and Psychiatry (tenured); Professor of Medicine/Infectious Diseases (tenured); Adjunct Professor of Neuroscience; (since 2019) E.B. Flink Vice Chair for Research, Department of Medicine

ii. Past:
   1. Professor of Medicine/Infectious Diseases (tenured) and first Associate Chair for Faculty Development, Department of Internal Medicine at the University of Cincinnati College of Medicine; Associate Professor of Clinical Medicine//Infectious Diseases (1995-2015)
   2. Associate Professor of Medicine/Infectious Diseases (1995), Johns Hopkins School of Medicine; Assistant Professor/Infectious Diseases (1990-1995)
   3. See attached CV for prior positions

e. **Honors and Memberships**

i. Honors
   1. 2020: You Make a Difference Award, Community Liver Alliance, Pittsburgh
   2. 2015: Cincinnati Healthcare Hero, finalist and winner, Community Outreach
   3. 2010: elected to Sigma Xi (science honor society)

4. 2010: Central Society for Clinical Research (member)
5. 2007: Michael Harris Humanitarian Award (inaugural recipient), Cincinnati
6. 2007-08: Leadership Cincinnati, Cincinnati Chamber of Commerce, Class XXI
7. 2006: Cincinnati Healthcare Hero, finalist and winner, Clinician
8. 2006: AIDS Volunteers of Cincinnati "Diva of Honor" Award
9. 2003: Constance B. Wofsy Women's Health Investigator Award
10. 2001-present: Selected by peers to be listed in "Best Doctors"
11. 1988: National Institutes of Health Award of Merit
12. 1981-82: Pillsbury Fellowship
13. 1980-82: Housestaff Representative, Committee on Admissions, Rush Medical College
14. 1979: Janet M. Glasgow Scholarship Achievement Citation, American Medical Women's Association, Rush Medical College
15. 1978: Alpha Omega Alpha (medical honor society, elected 3rd year), Rush Medical College
16. 1976-79: Student Representative, Committee on Admissions, Rush Medical College
17. 1967-69: New York State Fellow for Advanced College Teaching
18. 1967: General Honors in the College and Honors in Major Field (Russian Civilization), University of Chicago
19. 1967: Woodrow Wilson Fellowship semi-finalist, University of Chicago

ii. Memberships

1. Infectious Diseases Society of America (Fellow)
2. American College of Physicians (Fellow)
3. American Society for Microbiology
4. American Association for the Advancement of Science
5. American Academy of HIV Medicine (past Chair of the Board)
6. HIV Medical Association (current Chair of the Board)
7. International AIDS Society
8. International Network on Hepatitis in Substance Users
9. American Public Health Association
10. College on Problems of Drug Dependence
11. Sigma Xi (scientific honor society)
12. Alpha Omega Alpha (medical school honor society)
13. International Society for Antiviral Research
14. Society for Clinical Trials

f. **Publications**. For a list of my publications in the last ten years, please see attached CV.

III. COMPENSATION

I am being compensated for my work in this case at the following rate: $800 per hour. My compensation is not contingent on the outcome of this litigation.

IV. PRIOR TESTIMONY

I have provided testimony in the following legal matters during the last four years: MARZIEH SALEHI, M.D., Claimant vs. CEDARS-SINAI MEDICAL CENTER, a California nonprofit corporation, Respondent, JAMS Case No. 1220062143.

V. SUMMARY OF OPINIONS

The current opioid epidemic in the United States and West Virginia has its roots in misuse of prescription opioids. When access to prescription opioids was limited by changes in prescribing and the resulting increased cost of pills on the street, the ready availability of potent and less costly heroin triggered a transition to from pills to heroin, eventually leading to injection use among people who had become dependent on prescription opioids. This has resulted in the dramatic rise of opioid-related injection drug use (IDU) and an unprecedented loss of life due to opioid overdose in the United States, and especially, in West Virginia. Injection drug use which involves the introduction of unsterile drug prepared using contaminated materials delivered directly into the bloodstream through unclean skin (often after licking the needle prior to injection) has led to the syndemics of serious, life-threatening injection-associated infectious diseases caused by viruses, bacteria and fungi. These include Human Immunodeficieny Virus (HIV), hepatitis B and C viruses (HBV, HCV), and serious bacterial and fungal infections of the heart (endocarditis) and other organs. The lethality of these infections is evident in the subsequent development of the Acquired Immune Deficiency Syndrome (AIDS), cirrhosis and end-stage liver disease, and heart failure in people who inject drugs who are not promptly diagnosed and treated.

VI. OPINIONS

A. Human Immunodeficiency Virus (HIV)

1. What is HIV?

HIV is an RNA virus that belongs to the retrovirus family and is the smallest known disease-causing virus in humans. The term “retrovirus” denotes an RNA virus that creates an intermediate DNA form of its genetic material so that it can bond to human DNA and direct cell activities that in turn generate new RNA daughter viruses that bud from the infected cell. The primary target of HIV is the CD4+ T-lymphocyte (also known as a T4 cell or a T helper cell), a cell type that is central to normal functioning of the human immune system. As an RNA virus HIV is prone to generating mutations, which are genetic changes that may benefit the virus, such as mutations that confer resistance to existing antiretroviral drugs. HIV is transmitted by exposure to body fluids including semen and vaginal fluid, blood and breast milk. The most common routes of transmission are sexual (with receptive anal intercourse being riskier than vaginal intercourse), transfusion or exchange of blood and blood components, transplantation of infected tissue, mother-to-child (vertical transmission) during pregnancy and delivery, and breastfeeding.

The risk for acquiring or transmitting HIV through injection drug use is very high if an HIV-negative person uses injection equipment that has been used by a person living with HIV, because the needles/syringes may contain HIV-infected blood and there may be virus in the materials used to prepare drug for injection. Depending on temperature and other factors, HIV can survive in a used syringe for up to 42 days (Abdala 2000). Opioid use disorder can also increase the risk of sexual acquisition of HIV due to altered judgment regarding risky sexual behaviors, such as sex without a condom or the use of pre-exposure prophylaxis, having multiple partners, or transactional sex (trading sex for drugs, money, or other benefits). Sharing syringes is the second riskiest behavior for acquiring

HIV after receptive anal sex: there is a 1 in 160 chance of acquiring HIV every time an HIV-uninfected shares a needle/syringe that has been used by a person living with HIV (CDC IDU and HIV Risk 2020).

Globally, approximately 38.0 million (range, 31.6–44.5 million) people were living with HIV at the end of 2019, and 690,000 had died of HIV/AIDS-related illnesses that year (WHO 2020). At the end of 2018, an estimated 1,173,9000 people in the U.S. were living with HIV (CDC Factsheet 2020). Approximately 1.2 million people in the U.S. are living with HIV today, of whom approximately 14% are unaware of their diagnosis. In 2018, 37,968 people in the U.S. received an HIV diagnosis and there were 15,820 deaths (CDC 2020).

In the absence of antiretroviral therapy, persons living with HIV experience progressive immune dysfunction and typically start to experience non-specific symptoms, such as fatigue, weight loss, rashes and oral or vaginal thrush; however, some individuals remain asymptomatic for an extended period enhancing the possibility that they will not come to medical attention for testing. In the continued absence of a diagnosis and antiretroviral therapy, individuals will progress from HIV infection to Acquired Immune Deficiency Syndrome (AIDS) in an average period of 8 to 10 years. At this point, the total CD4 cell count will be less than 200/μL and they will be susceptible to any of 27 AIDS-defining conditions in the CDC's surveillance definition. These conditions are primarily "opportunistic infections" because they take advantage of a weakened immune system and do not ordinarily cause disease in immunologically intact persons, and several are neoplasms (forms of cancer) that also target immune-suppressed individuals, such as central nervous system (brain) lymphoma. Persons with untreated AIDS may experience a number of these opportunistic diseases before ultimately dying.

The development of potent combination antiretroviral therapies since 1996 can forestall immune damage if started soon after infection and can even provide significant benefit to those who have already progressed to AIDS although typically maximal benefit derives from earlier treatment. These potent combinations can suppress the amount of HIV in the blood (the "viral load") to levels below the limit of the assay's lowest detectable limit and is called "undetectable" in everyday parlance. However, there are assays used in research that can detect as low as a single copy of HIV RNA ("single copy assay"), so we know that the virus has not been eradicated (cured). If a person stops taking their combination treatment, the pre-therapy amount of HIV, termed the "set point", will come roaring back within days to weeks. Thus, maintenance of health is dependent upon lifelong adherence to combination therapy. (Mandell pp.1469-1547).

There are a number of approaches to prevention of HIV transmission via sex. An "undetectable" viral load is significant not only for maintenance of individual health but also for limiting transmission to sexual partners. Clinical trials have shown that using effective antiretroviral therapy (ART) to consistently suppress plasma HIV RNA levels to <200 copies/mL prevents transmission of HIV to sexual partners. Research has demonstrated that among HIV-discordant couples—where one has HIV and the other does not—that if the partner living with HIV has an undetectable viral load, sexual transmission does not occur, even in the absence of condom use (Cohen 2016). Clinical trials have shown that using effective antiretroviral therapy (ART) to consistently suppress plasma HIV RNA levels to <200 copies/mL prevents transmission of HIV to sexual partners. When ART is used to prevent HIV transmission, this strategy is called "treatment as prevention" (TasP), commonly referred to as Undetectable = Untransmittable or U=U (DHHS Adult and Adolescent Guidelines 2020). In addition to virologic control in the index partner, combination antiretroviral therapy can be used either before sexual contact (pre-exposure prophylaxis, or PrEP) or soon after an unprotected sexual exposure (post-exposure prophylaxis, or PEP). The Centers for Disease Control and Prevention have periodically updated guidelines for PrEP and PEP as additional data become available (CDC March 2018, CDC 2016).

Only one large, randomized, placebo-controlled trial to date has examined the prevention of HIV transmission among people who inject drugs (PWID). That study compared tenofovir to placebo among 2,413 PWID in Bangkok and found that HIV incidence was reduced by 48.9%; protection was 74% among those participants with detectable tenofovir levels (Choopanya 2013). However, reported syringe sharing decreased from 18% at baseline to 2% by month 12, suggesting that this study may not be generalizable to PWID with greater levels of syringe sharing.

2. Persons living with diagnosed HIV in the United States and in West Virginia

The introduction of needle/syringe exchange early in the HIV/AIDS epidemic resulted in a sharp decline in the proportion of cases associated with IDU in the 1990s-early 2000s. However, from 2014 to 2018, there was an overall 9% increase in new HIV diagnoses among PWID in the U.S., with increases of 10% in men and 7% in women (https://www.cdc.gov/hiv/statistics/overview/index.html, accessed 7/20/20; https://gis.cdc.gov/grasp/nchhstpatlas/charts.html; accessed June 27, 2020- see figure). In 2015 the demographics of HIV among PWID reached an inflection point where more new HIV diagnoses occurred among whites rather than in any other racial or ethnic group, younger individuals (13-34 years), those residing outside large central metropolitan areas (CDC November 2018, Lyss 2018).

In 2014-2015, the Scott County HIV outbreak in southeastern Indiana marked the first such outbreak in the rural U.S. and was a wake-up call that HIV outbreaks could occur outside of metropolitan areas. Five percent of the community – 181 persons, of whom 42.5% were women, 98.9% white, and 91.9% PWID – were diagnosed with HIV (Peters 2016). In response, the CDC conducted a study to assess vulnerability to HIV and/or hepatitis C outbreaks in rural areas based on the characteristics of the Scott County outbreak and identified 220 rural counties across the U.S. at highest risk. In that assessment, more than 50% of the vulnerable counties were located in central Appalachia, with the largest total number located in Kentucky and West Virginia. In fact, West Virginia had the highest proportion of at-risk counties in the U.S.: 28 of 55 (51%) (Van Handel 2016).

By the end of 2018, there were 1,173,900 people in the U.S. and dependent areas living with HIV, 86% of whom knew their diagnosis. That year there were 37,968 new HIV diagnoses, with the largest proportion, 51%, in the South, for a rate of 15.6 per 100,000 population (note that for CDC statistics, West Virginia is counted as being in the South). Among new HIV diagnoses, 7% occurred among PWID, 68% occurred in adolescents and younger adults 13-44 years old, 45% among whites and 28% among women.

Although there have always been cases of HIV in West Virginia, the statewide incidence and prevalence have historically been low and primarily due to sexual transmission. From 2013 to 2017, the average annual number of new cases in the state was 77, and the average annual number in Cabell County was 7 (https://oeps.wv.gov/hiv-aids/documents/data/WV_HIV_2013-2017.pdf; accessed 8/2/2020). At the end of 2014 the prevalence of HIV in Cabell County remained "…comparatively low compared to other areas of the state" although it was noted that the increase in the number of HCV cases required "ongoing" evaluation of HIV/AIDS trends (CHHD 2015, p. 30).

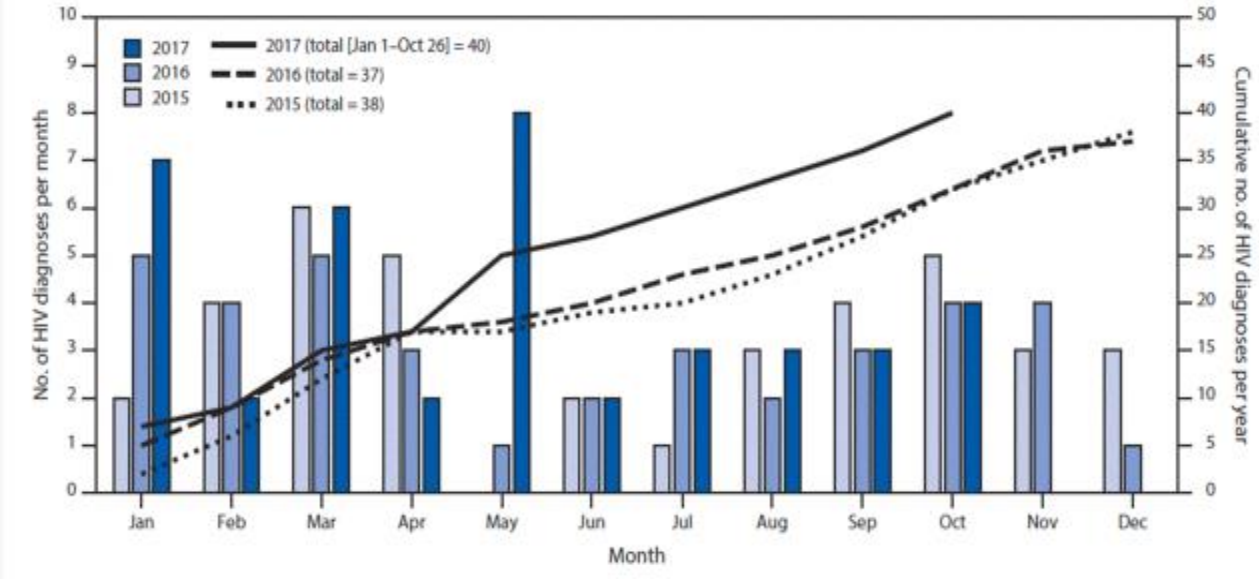
From January to July 2017, 10 cases of HIV infection were identified in three counties where HIV diagnoses typically range from 6 to 13 annually and, despite the fact that injection drug use is a major public health concern in these counties, no syringe services programs were available (Evans 2018). Nine of the 10 were men who have sex with men (MSM), two of whom also had a history of IDU. Contact tracing identified another 47 cases across a total of 15 southern coalfield counties (Evans 2018), 14 of which were among the nation's 220 counties identified by the CDC as particularly vulnerable to rapid

spread of HIV and/or HCV infections through IDU (Van Handel 2016). All 57 cases were linked either epidemiologically or through HIV molecular analysis. Almost half (49%) were under age 30, and 14% were MSM who reported IDU (9%) or persons whose primary risk for HIV was IDU (5%). Of interest, 23% could either not be reached or would not disclose potential risk(s) for HIV acquisition (Evans 2018). A study to evaluate risk interviewed 39 of these cases and 39 contacts about past-year risk behaviors and elicited sexual, IDU, and social contacts; contacts were tested for HIV and potential risk behaviors were assessed. Overall, 13/78 (17%) injected drugs in the past year. Of 19 diagnosed in 2017 who had detectable virus, 9 (47%) had at least one sexual or IDU contact with negative or unknown HIV status; 2 of these 9 had injected drugs and shared equipment, and 1/9 had at least 1 partner who did so (Bradley 2019). These data reflect the growing incidence of HIV among PWID in southern West Virginia which has become more marked over time.

In 2018, the state HIV total rose to 87 with 39 (45%) attributed to IDU; in 2019 the total increased yet again to 146 with 91 (62%) attributed to IDU; and in the first 6 months of 2020, there have been 50 new HIV diagnoses, with 34 (68%) attributed to IDU. Thus, while there has been an increased proportion of new HIV diagnoses among PWID nationwide over the past several years, since 2017 there has been a significant increase in the number of new HIV cases in West Virginia attributable to IDU, which is now the dominant route of HIV infection in the state. The majority of these cases have occurred in Cabell County [see below](https://www.cdc.gov/hiv/statistics/overview/index.html; accessed 7/20/20).

Subsequent to the CDC vulnerability assessment, a state-specific assessment was undertaken by the West Virginia Bureau for Public Health. Variables associated with proxy for IDU in addition to those used by the CDC were used to reflect West Virginia-specific data. Of the ten variables included in the model-building process, three were significantly associated ($p<0.05$) in the multivariable model for increased vulnerability to rapid spread of HIV and HCV: self-reported disability, lack of health insurance, and drug-related hospitalizations (Batdorf 2020- see figure). There was considerable overlap between the CDC and West Virginia vulnerability assessments, with the West Virginia assessment including two additional counties, Pocahontas and Greenbrier)(Batdorf 2020).

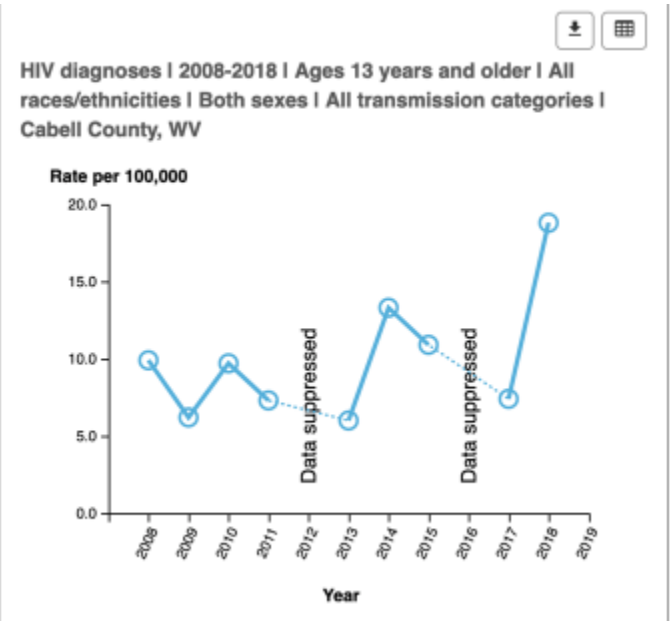
FIGURE. Number of HIV diagnoses per month and cumulative number of diagnoses per year — 15 West Virginia counties, 2015–2017



3. Persons living with diagnosed HIV in Cabell County and City of Huntington.

From 2013 to 2017, there was an annual average of 7 new diagnoses of HIV in Cabell County (https://oeps.wv.gov/hiv-aids/documents/data/WV_HIV_2013-2017.pdf; accessed 8/2/2020). An increase was noted in 2014 with a sharp increase in the number of HIV diagnoses in 2018, when the total reached 17, with 13 (76%) among PWID (https://oeps.wv.gov/hiv-aids/documents/data/WV_HIV_2018-2020.pdf; https://gis.cdc.gov/grasp/nchhstpatlas/charts.html- see figure). In 2019, there were 69 new cases, with 63 (91%) among PWID (Ibid.). In the first 6 months of 2020, Cabell County has had 17 new HIV diagnoses, with 16 among PWID (94%) (Ibid.). Thus, over the past 2.5 years there has been a dramatic increase in new HIV diagnoses among Cabell County residents with the vast majority occurring in PWID (https://oeps.wv.gov/hiv-aids/pages/default.aspx).

https://gis.cdc.gov/grasp/nchhstpatlas/charts.html



4. Number of new HIV cases due to IDU per year.

The proportion of new HIV diagnoses in the U.S. has been increasing since 2014 (https://gis.cdc.gov/grasp/nchhstpatlas/charts.html). Since October 2019, West Virginia has seen the emergence of HIV among PWID in other parts of the state such as Kanawha County that are not linked to the Cabell outbreak (Health Advisory 162: HIV Infections Among People Who Inject Drugs – Additional Area Seeing Increase, Others Vulnerable). As a result, as of October 10, 2019, the West Virginia Bureau for Public Health started categorizing new cases of HIV according to the person's county of residence at the time of diagnosis to eliminate duplication of cases across jurisdictions, and to facilitate determination of risk so that appropriate public health actions can be taken at the local level. In Cabell County, at the time of this switch in reporting, there were a total of 81 new HIV diagnoses from January 1, 2018 to October 9, 2019, of whom 73 (90%) resided in Cabell County at the time of diagnosis.

There have been a total of 163 new HIV diagnoses in West Virginia attributed to injection drug use from January 1, 2018 to July 1, 2020, with the majority in Cabell (92) and Kanawha (29) counties (Health Advisory 162: HIV Infections Among People Who Inject Drugs – Additional Area Seeing

Increase, Others Vulnerable). This is being driven by the sharing of injection drug equipment as well as high-risk sexual practices (*Ibid.*). Other counties have seen smaller numbers of cases: Mononghalia-6, and Mercer, Ohio and Wayne, each with 5. The other 21 new HIV diagnoses are scattered among 13 other counties, each with 1-4 cases.

5. Standard Treatments for HIV

The standard of care for HIV infection is to start potent combination antiretroviral therapy consisting of at least two drugs from different chemical classes as soon as possible, in both acute and chronic cases. U.S. Guidelines provide a number of recommended initial regimens for patients that have no drug resistance. The readiness of the patient is essential because inconsistent adherence to prescribed medication can lead to drug resistance, which generally requires more complex regimens that may less well tolerated. Since HIV cannot be cured, the goal of treatment is to suppress the amount of virus in the blood to a level that is below the lower threshold of the assay being used, or in everyday parlance, to an "undetectable" level. The generally accepted current threshold is less than 200 copies of virus per mL; although more sensitive tests exist they are primarily used in the research setting. When a person living with HIV achieves virologic suppression (an "undetectable viral load"), s/he benefits from a strengthened immune system and cannot transmit the virus to an unprotected sexual partner ("treatment as prevention")(Panel on Antiretroviral Guidelines 2020). Individuals who receive their diagnosis when they already have advanced HIV disease, or AIDS, should receive prophylaxis for common opportunistic infections dictated by the level of damage to their immune system as measured by their total CD4 (T4 cell, T helper cell) count. Once the CD4 cell count increases above the threshold of risk for a specific opportunistic infection for at least a three-month period, the prophylactic agent(s) may be discontinued (Guidelines for the Prevention and Treatment of Opportunistic Infections 2019) without risk.

B. Hepatitis C Virus (HCV)

1. What is HCV?

i. The Liver and Hepatitis C

The liver is the chemistry plant of the body. The liver removes toxins from the blood, makes proteins that regulate blood clotting, makes albumin that is the most common protein in the blood, produces bile to absorb fats and vitamins from food, stores glucose as glycogen for energy, and is the most important site for the metabolism of most drugs. Put simply, a human being cannot live without a liver due to the essential role it plays in ensuring the proper functioning of multiple systems in the body.

Chronic hepatitis C is a liver disease caused by the hepatitis C virus (HCV). HCV is an RNA virus—meaning that its genetic material is composed of RNA and not DNA—primarily spread by contact with the blood of an infected person, but it can also be transmitted sexually, primarily among men who have sex with men, and from pregnant women to their newborn infants. There is no preventive vaccine for HCV. A CDC study showed that ***annual hepatitis C-related mortality in 2013 surpassed the total combined number of deaths from 60 other infectious diseases reported to CDC, including HIV,*** pneumococcal disease, and tuberculosis (Ly 2016). Hepatitis C is now the third leading cause for liver transplantation in the U.S. (Infection Control Today 2018).

Hepatitis C is a disease with two significant elements to its pathophysiology. In diagnosing or treating HCV, the activity of the infection and the inflammation and scarring that it causes both play significant roles in disease expression. The activity of the infection (also known as the "viral load," the number of viral particles that can be measured in the blood) and the progression of inflammation are not

necessarily linked – that is a high viral load does not necessarily correlate with the degree of inflammatory damage, and vice versa. The only way to determine the extent of the inflammation is by examining a biopsy of the liver. Inflammation leads to fibrosis, the medical term for scarring. Initially fibrosis is confined to specific areas of the liver, but as fibrosis worsens it will eventually lead to widespread scarring, termed cirrhosis. As cirrhosis worsens and the patient becomes medically decompensated from excessive liver damage, the patient will have reached end-stage liver disease, which will ultimately result in death in the absence of a liver transplant. Hepatocellular carcinoma (liver cancer) is another complication of cirrhosis, which can also be fatal.

The severity of HCV-related liver disease is described by its stage and grade. The stage refers to the amount of scarring or fibrosis of the liver. The grade refers to the amount of necrosis, or liver cell death, and inflammation. There are five stages, zero through four, with zero indicating normal liver architecture. The initial stage of cirrhosis of the liver is termed stage 3 (early, or incomplete cirrhosis), with stage 4 being established cirrhosis. In cirrhosis, scar tissue replaces normal healthy liver tissue, blocking the flow of blood through the liver, thus preventing the liver from functioning normally. This can lead to swollen blood vessels in the abdomen and the esophagus, known as varices, and to an enlarged spleen that is engorged with blood that cannot circulate normally through the liver, known as splenomegaly. The level of inflammation is important because it may be correlated with the development of fibrosis. There are five grades of liver disease: grade 0 is no inflammation while grade 4 is severe.

It is important to note that progression of liver disease is non-linear, which means that the rate of progression is unpredictable. There can be periods of time where there is little or no progression of the disease followed by rapid periods of decline in liver status.

2. Persons living with diagnosed HCV in the United States and in West Virginia and connection to IDU

Persons with Substance Use Disorder account for 68-80% of HCV infections in developed countries (Talal 2017). It is estimated that there are 3.5–5.2 million people in the U.S. who currently have HCV infection with prevalence estimates among PWID of up to 90% (Hernandez 2011). From 2006 to 2012, HCV incidence increased among young adults with more than two-fold annual increases in nonurban areas (Suryaprasad 2014). In the same period, the incidence of acute HCV in central Appalachia (West Virginia, Kentucky, Virginia and Tennessee) increased 364% among young adults 30 years old and younger (Zibbell 2015).

In 2018, 3,621 acute HCV cases were reported to the CDC, resulting in an estimated 50,300 new infections (95% CI: 39,800–171,600) after adjusting for case under-ascertainment and under-reporting. The reported acute HCV case count corresponds to a rate of 1.2 cases per 100,000 population; this is a greater than 71% increase from the rate of 0.7 cases per 100,000 population in 2014. Over 65% of acute HCV cases in 2018 were among young adults 20-39 years old. Among the 1,535 (42%) reported acute cases that included injection risk information, 1,102 (72%) reported IDU (CDC Viral Hepatitis Surveillance 2020).

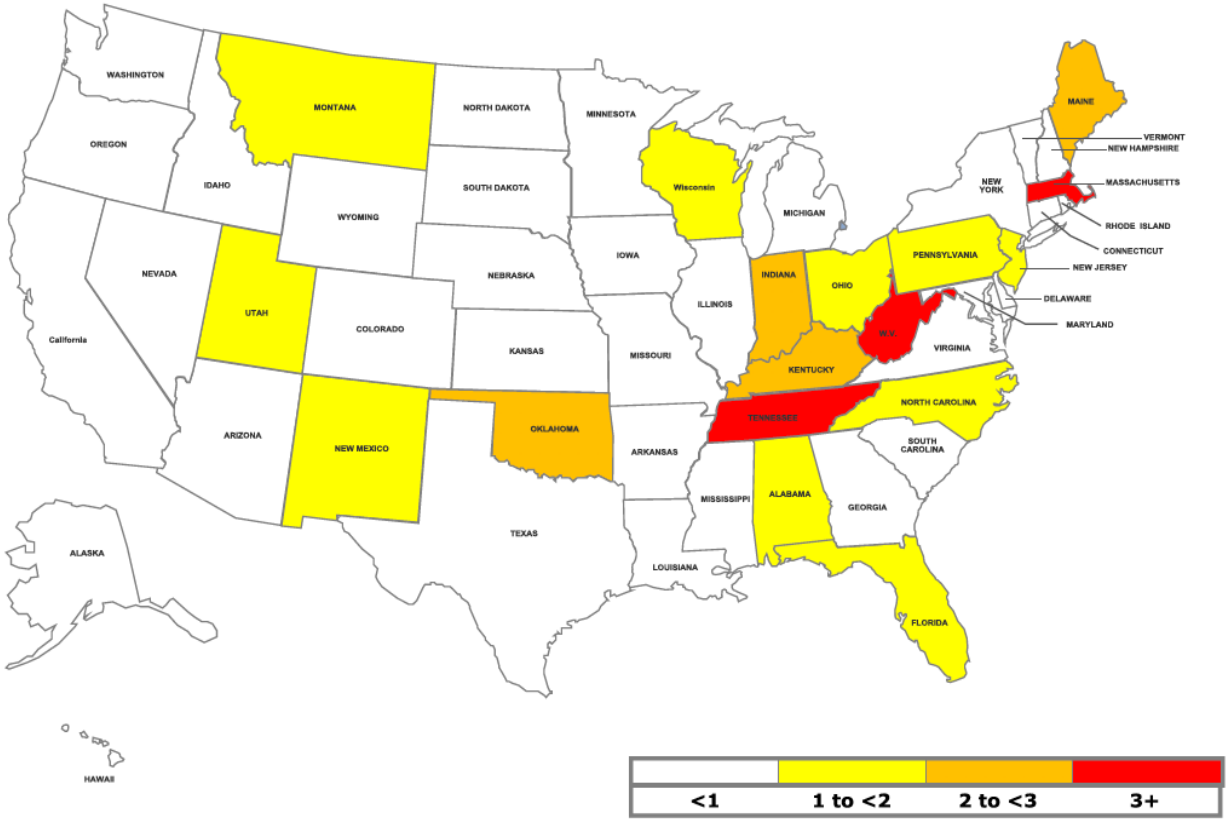
For many years, West Virginia has had among the highest rates HCV infection in the U.S. The CDC Nationally Notifiable Disease Surveillance System (NNDSS) reported that between 2010 and 2015, West Virginia had the second highest annual incidence of acute HCV (https://oeps.wv.gov/hepatitis/documents/data/Summary_2016_Acute_HBV-HCV.pdf), a ranking that persists in 2018 (CDC July 2020) and the second highest rate of HCV infection at 3.4 per 100,000 population in the U.S. Since 2010, the incidence of acute HBV and acute HCV has increased 213% and 209%, respectively (https://oeps.wv.gov/HCV/documents/data/Hepatitis-Report-2016.pdf). Thus, West

Virginia bears one of the highest rates of individuals progressing to chronic liver disease due to viral hepatitis. Studies have linked the dramatic rise in HCV cases to the injection opioid epidemic in the U.S., especially in central Appalachia, where 1,377 cases in West Virginia, Virginia, Tennessee and Kentucky were recorded from 2006 to 2012. This represents a 346% increase that was tied to opioid injection among whites in rural and small urban areas, with IDU identified as a risk factor in 73% (Zibbell 2015). Of individuals who acquire acute HCV, 75-80% will have chronic HCV infection; 60-70% will develop chronic liver disease; 5-20% will eventually develop cirrhosis, a progressive disease where scar tissue forms and prevents the liver from functioning properly, usually over a period of 20-30 years; and 1-5% will die from the consequences of chronic infection, which include end-stage liver disease and liver cancer.

An increase in the number of infants born to chronically HCV-infected women in Kentucky from 2011 to 2014 has raised concerns about vertical transmission of HCV from mother to newborn (Koneru 2016). From 2006 to 2014, a 3.4-fold increase in acute HCV and a doubling of past or present cases among women of childbearing age (15-44 years old) was seen in the U.S., with the highest proportion of acute cases occurring in southern states that included West Virginia (Ly 2017). Non-Hispanic white women accounted for 57% of the acute cases and among women for whom risk information was available, 63% acknowledged IDU. In each of these years, an estimated 1,700 infants were infected by vertical transmission (Ly 2017). Vertical transmission is a particular concern because the majority of children born to HCV-infected mothers who are at risk for vertical transmission of HCV are not subsequently screened (Kuncio 2016). There were 214 perinatal HCV cases reported to CDC in 2018, which is the first year that standardized surveillance for perinatal HCV was conducted by states (CDC Hepatitis Surveillance 2020).

Overall, use of street drugs (non-injection) and injection drug use were the most common risks for acute HCV in West Virginia in 2016, and was the most common route of acute infection in adults <19-39 years old (Hepatitis B and Hepatitis C Infection in West Virginia 2018).

Figure 4. Rate of acute HCV infection per 100,000 population, U.S., 2016 (Source: CDC)



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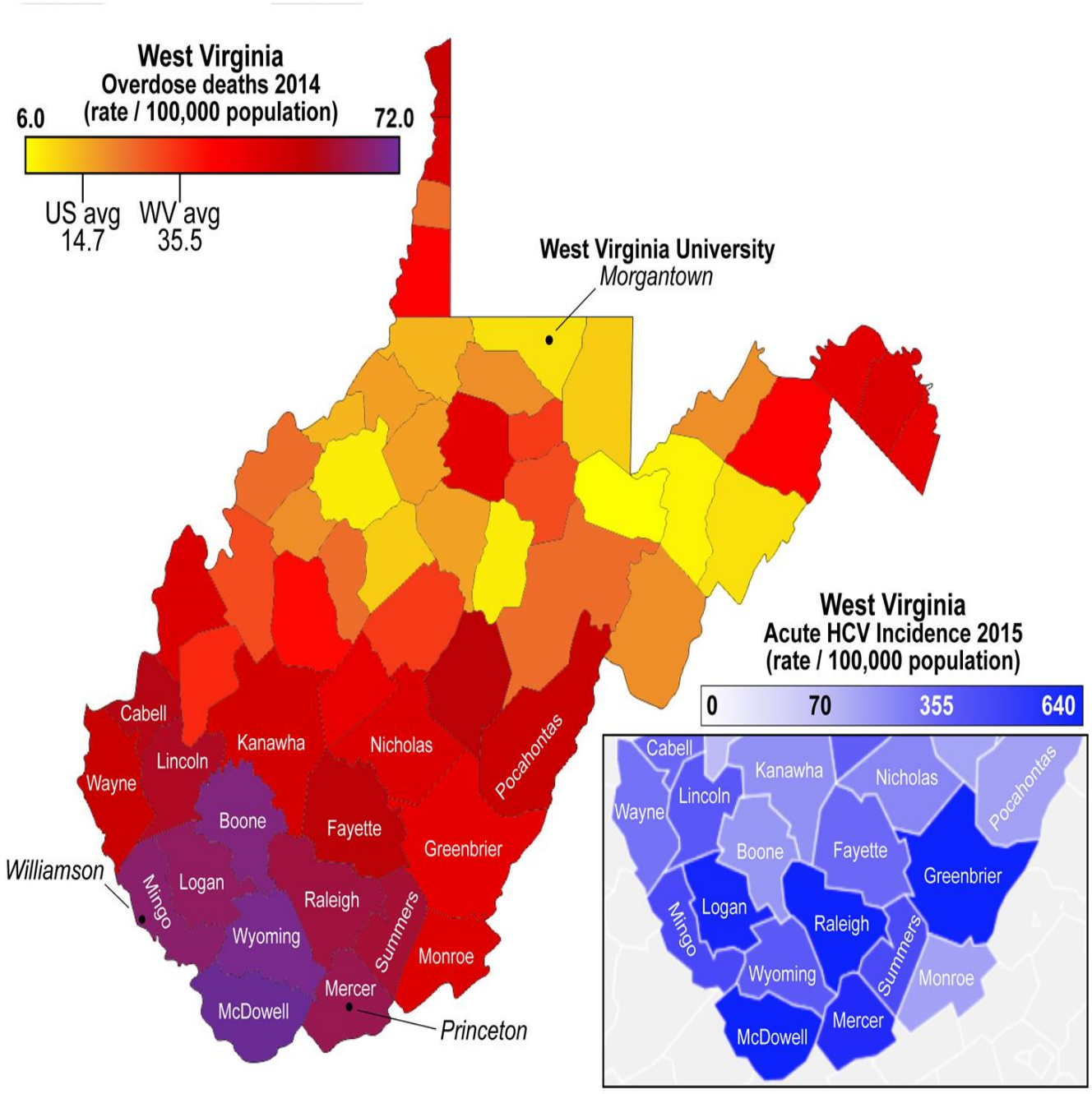


3. Number of reported acute (new) HCV cases per year (2005 to 2017) and Persons living with diagnosed HCV in Cabell County and City of Huntington

From 2007 to 2012, Cabell County's rate of confirmed acute HCV ranged from 0 to 1 per 100,000 population, but starting in 2013 the rate doubled to 2.1 and then doubled again to 4.1 in 2015 (https://oeps.wv.gov/HCV/documents/data/incidence_acute_hcv_2007-2015.pdf); from 2012 to June 2015, confirmed chronic HCV cases doubled among those less than 25 years old in this 3.5 year period (CHHD 2015). In 2016, Cabell County had one of the highest rates of acute HCV in West Virginia, 10.3/100,000 population—double the rate for the entire state at 5.1/100,000 (https://oeps.wv.gov/HCV/pages/hcv_data.aspx)--as well as one of the highest number of reported cases of chronic HCV at 480 in the entire state of West Virginia (Hepatitis B and Hepatitis C Infection in West Virginia 2018).

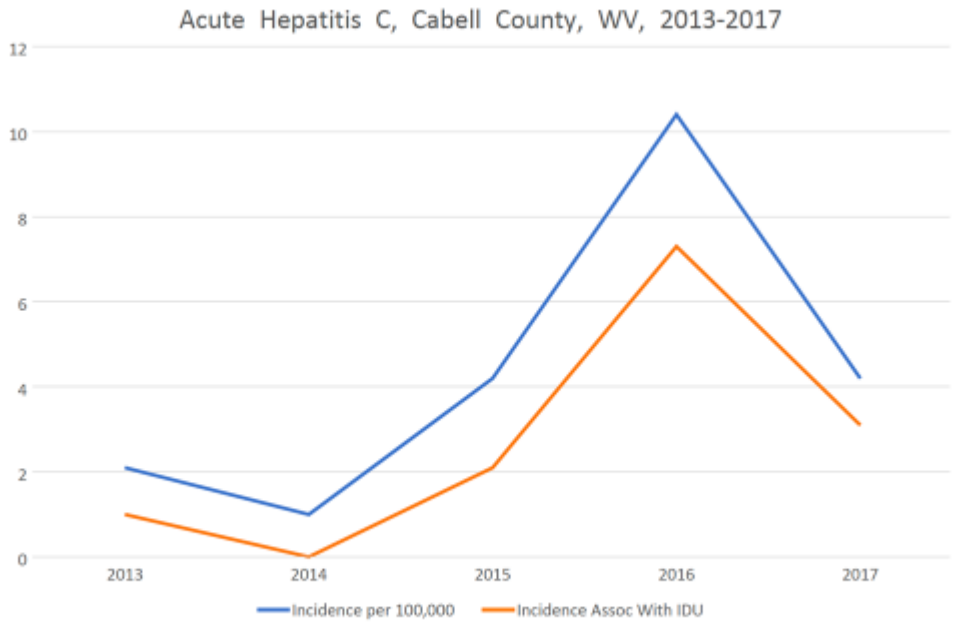
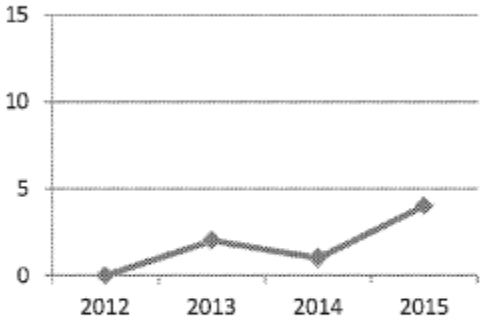
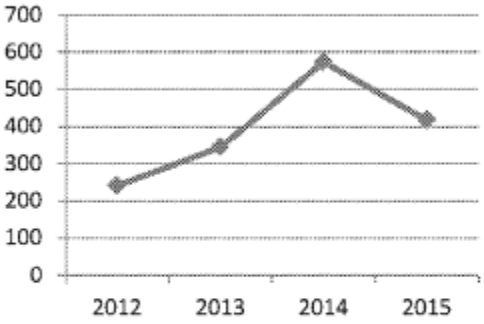


Figure 46. Acute, confirmed cases of Hepatitis C reported in Cabell County, 2012-2015.



Source: Cabell-Huntington Health Department

Figure 47. Chronic, confirmed cases of Hepatitis C reported in Cabell County, 2012-2015.



Source: Cabell- Huntington Health Department

CHHD, 2015, p. 32

4. Current Standard of Care for Treating Chronic HCV

Previously, because the possibility of curing chronic hepatitis C was very limited (less than 50%) with prolonged, toxic treatment of 24-48 weeks' duration with injectable interferon and later, with inferferon plus oral ribavirin, most physicians relied on liver pathology to guide treatment, focusing on the patients with more advanced disease. Recently, the development of combination oral medication (referred to as Direct Acting Agents, or DAAs) has been shown to produce cures in >95% of patients with only 8 to 12 weeks of well-tolerated treatment. As a result, the recent joint guidelines published by the Infectious Diseases Society of America (IDSA) and the American Association for the Study of Liver Disease (AASLD), recommend that all patients with chronic hepatitis C should be treated to preserve liver function, to prevent the development of fibrosis and cirrhosis, to decrease morbidity and mortality, and to decrease the transmission of hepatitis C to others.

The goal of current hepatitis C treatment is to eliminate the virus to avoid progression of liver disease. This is achieved when there is a sustained virologic response (SVR12) to treatment. SVR12 indicates the eradication of HCV from the body when the HCV viral load is undetectable 12 weeks after the conclusion of treatment. A patient who achieves an SVR12 has improved life expectancy and a lower chance of cirrhosis, liver cancer, and liver failure. Generally, the earlier treatment begins, before liver disease severity has progressed, the better the chance of obtaining a cure, although even patients with decompensated cirrhosis have achieved SVR12. Achievement of SVR12 has also been shown to be cost-effective, as cirrhosis and end-stage liver disease result in frequent hospitalizations for management of the complications of disease, such as ascites (massive accumulation of fluid in the abdomen) and generalized edema, gastrointestinal bleeding, confusion and frank encephalopathy, and spontaneous bacterial peritonitis, among other complications.

Treatment depends on a patient's genotype, or strain. HCV has six genotypes, with genotype 1 being the most common in the United States. However, in West Virginia there is a significant proportion—approximately 30%—of individuals who are chronically infected with genotypes 2 and 3, that are more difficult to cure. The new combination oral treatments for HCV called Direct Acting Antivirals (DAAs) consist of combinations of 2 or 3 DAAs. One combination, called Harvoni®[1], has been shown to cure genotype 1 at a 99% success rate, regardless of race, age, or response to prior treatment. There are now several pangenotypic treatment options that can cure all six genotypes. For example, clinical trials of Epclusa® and Mavyret® show cure rates ranging from 95% to 100% for all six genotypes.

Several studies have shown that efficacy—i.e. the proportion of individuals who achieve a sustained virologic response to modern DAA therapy—among PWID is not different from the non-drug using population (Dore 2016, Grebely 2016). From both individual and public health standpoints, the goal of curing HCV is important. Once a person with minimal-to-no liver fibrosis is cured, s/he is no longer at risk of end-stage liver disease, cirrhosis or hepatocellular carcinoma due to HCV; those who are cured at the point where they have considerable liver fibrosis (stage 3 or 4) have a reduced risk but need to be monitored semiannually for possible adverse outcomes. And once a person is cured, s/he can no longer transmit it to others, thus limiting the further spread of this epidemic. Thus, it is important to cure HCV not only to preserve the liver function of the person suffering from the disease, but also to limit the spread of the virus to others.

[1] Although I have received a grant from Gilead Sciences to prevent HIV in women, the parent company of Harvoni®, it in no way influenced my opinion. I have suggested Harvoni® because ODRC already has Harvoni® listed in its formulary, but other drug combinations are available. The grant from Gilead Sciences is to study Pre-Exposure Prophylaxis to prevent HIV acquisition in U.S. women at high risk. It is a project focused on HIV prevention and does not involve hepatitis C or Harvoni®.

C. HIV and HCV Coinfection

1. Significance

Coinfection with HIV and HCV worsens the outcomes for both infections. HIV/HCV-coinfected patients suffer from more liver-related morbidity and mortality, nonhepatic organ dysfunction, and overall mortality than HCV-monoinfected patients (Lo Re 2014). Even in the era of potent combination antiretroviral therapy, HIV infection remains independently associated with advanced liver fibrosis and cirrhosis in patients with coinfection (Fierer 2013, Kirk, 2013).

2. Pathogenesis of the HIV/HCV clusters

The majority of HIV/HCV coinfections occur among people who inject drugs and men who have sex with men, due to the efficiency of transmission via blood and anal sex. In the Scott County HIV outbreak, described above, 92.3% were coinfected with HCV (Peters 2016).

3. Rate of HIV coinfection with HCV United States and in West Virginia

Nationally, coinfection with HIV and HCV is common (50%–90%) among HIV-infected PWID injection drug users, but because West Virginia has been a low prevalence state the coinfection rate is generally low (https://oeps.wv.gov/hiv-aids/Documents/data/WV_HIV_Epi_Profile_2017.pdf (P. 47)).

A cross-sectional study covering 2012-2015 showed 7.9% (n=164) of the 2,089 people living with HIV in West Virginia were coinfected with HCV (Ibid. p. 48). Cabell, Raleigh and Preston counties had the second highest number of coinfected persons, ranging from 10-22, while Kanawha County had the highest number (Ibid. see figure). HCV coinfection was most common among PWID (Ibid. see figure).

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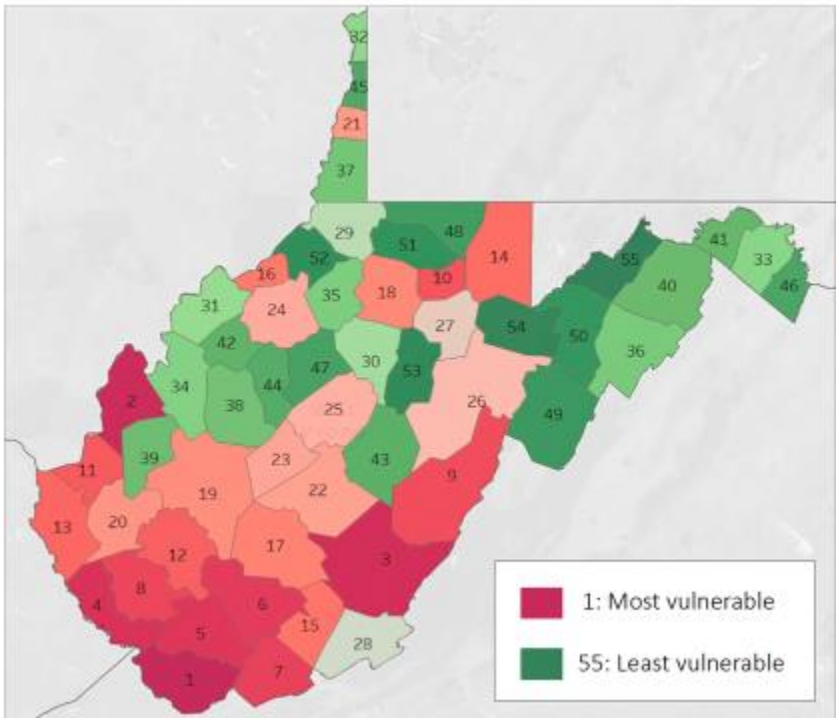
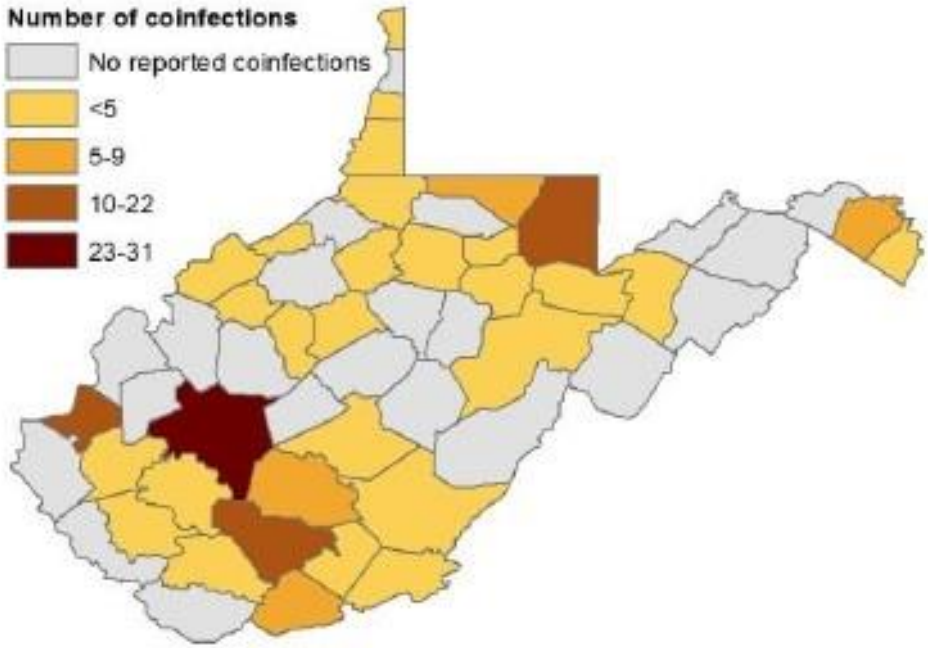
WV Vulnerability assessment for HIV & HCV



4. Rate of HIV coinfection with HCV Cabell County and City of Huntington

Figure 36. Number of HIV/HCV coinfections by county in West Virginia, 2012–2016*



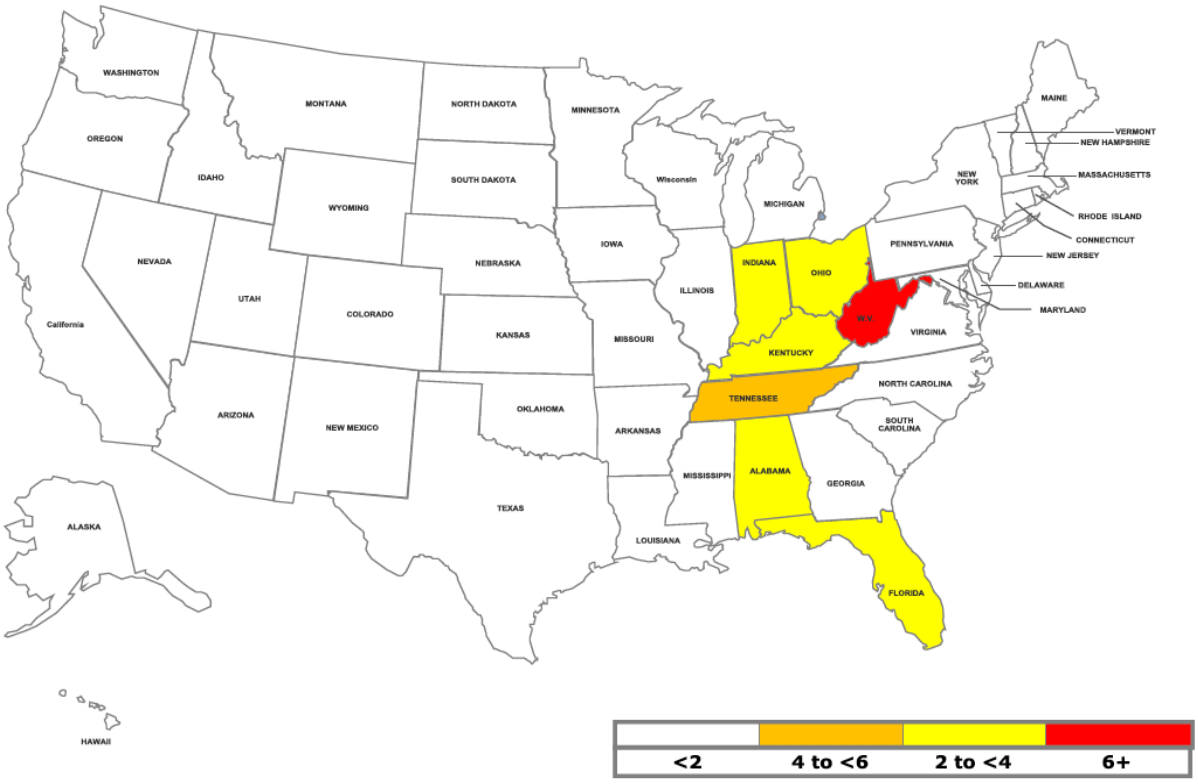
*federal prisoners included

D. Hepatitis B

1. What is Hepatitis B?

Chronic hepatitis B is a liver disease caused by the hepatitis B virus (HBV). Unlike HCV, HBV is a DNA virus—meaning that its genetic material is comprised of DNA—that can be spread in several ways: by contact with the blood of an infected person; sexually, both among men who have sex with men and heterosexuals; through ingestion of contaminated seafood; and from pregnant women to their newborns. Unlike HCV, a much smaller proportion of individuals who acquire acute HBV go on to develop chronic disease, they are also at risk for further progression to cirrhosis, end-stage liver disease and hepatocellular carcinoma. The total prevalence of chronic HBV infection in the United States at 2.2 million (Kim 2018).

Figure 3. Rate of acute HBV infection per 100,000 population, U.S., 2016 (Source: CDC)



2. Connection between Hepatitis B infections and IDU

The CDC Nationally Notifiable Disease Surveillance System (NNDSS) reported that between 2010 and 2015, West Virginia had the highest annual incidence of acute HBV (https://oeps.wv.gov/hepatitis/documents/data/Summary_2016_Acute_HBV-HCV.pdf), a ranking that persists in 2018. West Virginia also likely bears the highest rate of individuals progressing to chronic HBV, although the proportion who progress to chronicity is much smaller with HBV. Like HCV, studies have also linked the rise in HBV cases to the injection opioid epidemic in the U.S., especially in central Appalachia. In a study from 2006-2013 in West Virginia, Kentucky and Tennessee, there was an overall 114% increase in HBV diagnoses occurring after 2009 in whites, ages 30-39, reporting IDU (all, $p<0.001$), but no difference in gender, with 42% occurring in non-urban areas (Harris 2016). Low HBV vaccination rates seen in young adults contributed to this increase, which parallels the simultaneous increase in acute HCV in these same states. The authors concluded that "The concurrent increase in reports of acute HBV and HCV infections, as well as an increase in IDU reported among this population is concerning." (Harris 2016). Overall, use of street drugs (non-injection) and injection drug use were the most common risks for acute HBV in West Virginia in 2016 (Hepatitis B and Hepatitis C Infection in West

Virginia 2018). Like HIV/HCV coinfection, the HIV/HBV coinfection rate is relatively low due to the low prevalence of HIV in the state. From 2012-2015, coinfection most commonly occurred in young adults 20-29 years old and the most common route of infection was male-to-male sex (45%), followed by IDU (19%)(https://oeps.wv.gov/hiv-aids/Documents/data/WV_HIV_Epi_Profile_2017.pdf).

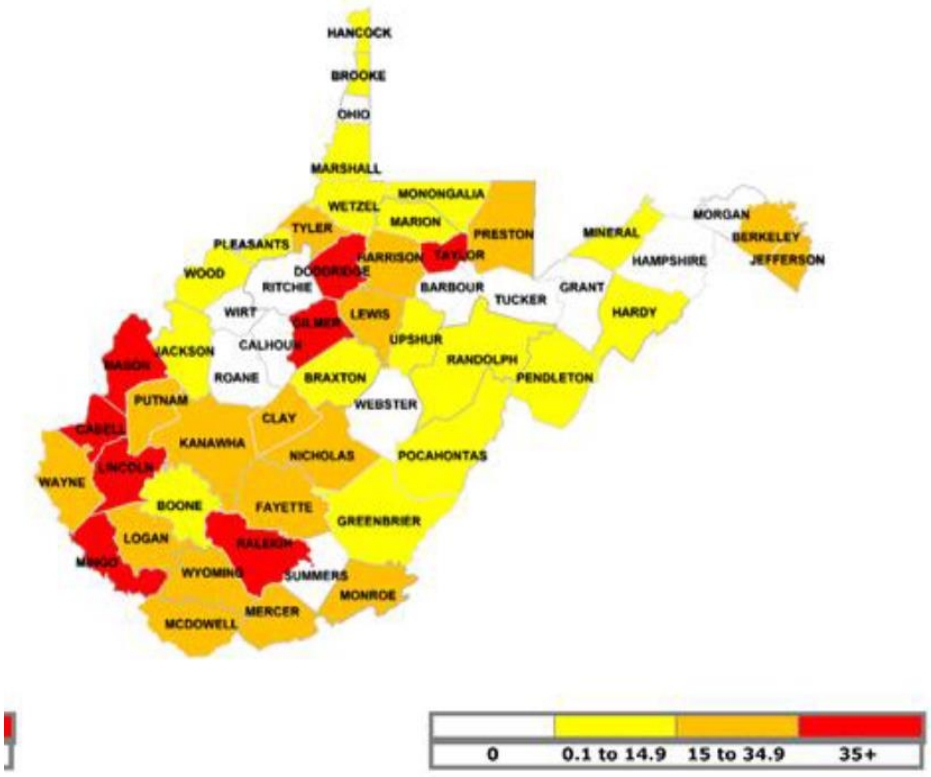
3. Hepatitis B in West Virginia and Cabell County

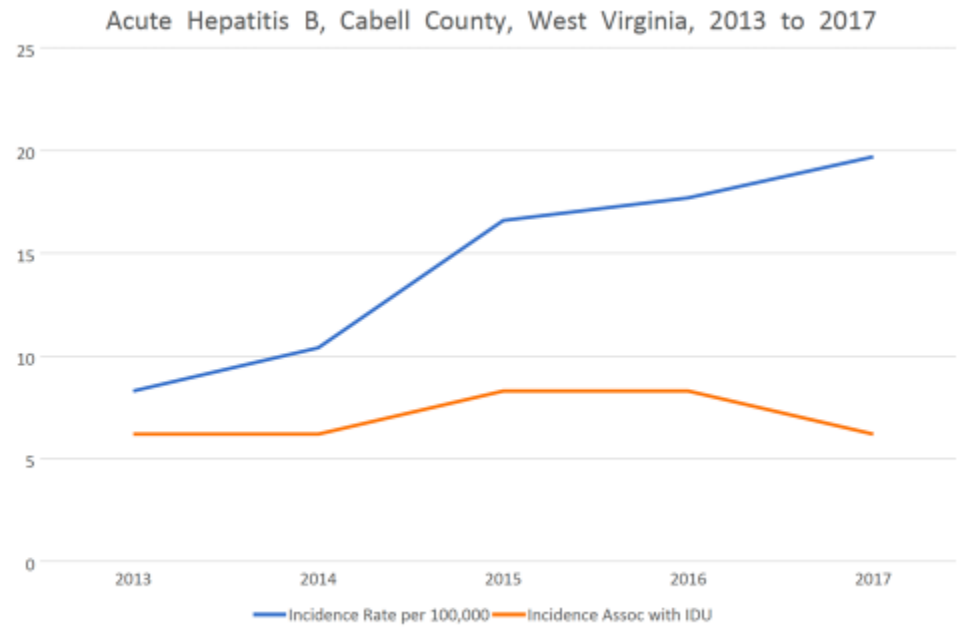
The number of newly reported chronic HBV cases in West Virginia has increased steadily every year; over the 10-year period from 2007 to 2016, the total increase was 291% (Hepatitis B and Hepatitis C Infection in West Virginia 2018). From 2012 to June 2015, Cabell County consistently had 8-10 cases of acute HBV and one case of chronic HBV each year (CHHD 2015). In 2016, the rate of newly reported cases of chronic HBV was 12.9 per 100,000 persons. In 2016, Cabell County had one of the higher rates of acute HBV, 17.6/100,000 population, and one of the highest numbers of reported cases of chronic HBV at 43 in the entire state of (Hepatitis B and Hepatitis C Infection in West Virginia 2018).

A study similar to the one in women of childbearing age with hepatitis C positive serology using the national Quest Laboratory database was performed in women 15-44 years old with positive blood tests for hepatitis B. A familiar pattern of prominent increases in HBV diagnoses among women in Appalachian states was also seen (Kushner 2019). Between 2011 and 2016, 92 infants were identified as being born to HBV positive mothers, the majority of whom (65%) were identified in 2014-2016; 5 (5.4%) infants were infected with HBV (Hepatitis B and Hepatitis C Infection in West Virginia 2018).

Figure 6.

The Rate of Chronic Hepatitis B per 100,000 Population, West Virginia - 2016 (n=353)





Data Source: Cabell-Huntington Health Department, 2017 data preliminary

4. Prevention and Treatment of Chronic Hepatitis B

Unlike HCV, while HBV can be prevented by vaccination, it cannot be cured. Similar to HIV, HBV can be managed using lifelong oral medication to suppress the HBV viral load to levels below the assay's limit of detection, thus maintaining health and preventing progression of liver disease to cirrhosis and hepatocellular carcinoma.

E. Endocarditis

1. What is endocarditis?

Infective endocarditis (IE) is an infection of the lining of the heart (endocardium) and most frequently affects the valves that control the flow of blood in and out of the heart. Bacteria are the most common infectious cause; fungi are an unusual cause of IE, especially in persons who inject drugs (PWID)(Mandell, p. 1002).

2. Connection between infective endocarditis and IDU

The injection of unsterile drug using unsterile drug preparation and injection equipment through unclean skin deposits microorganisms directly into the bloodstream (bacteremia). Transient bacteremia can result in adherence to and invasion of an initially sterile but damaged surface of the valvular endocardium (Mandell p. 992-3). The bacteria that most commonly cause IE are organisms that normally reside on the skin, such as staphylococci, and the mouth, such as streptococci; these are readily introduced into the bloodstream by injection through unclean skin with unwashed hands and by licking the needle—all of which are common injection behaviors. As drug is injected into a vein that traverses the right side of the heart first, right-sided IE is typical among PWID, but in some series PWID have predominantly had left-sided disease. [The right side pumps to the lungs and is the low-pressure

side of the heart; the left side pumps to the rest of the body and is the high-pressure side. When a left-sided valve fails, acute congestive heart failure occurs and is a surgical emergency.] Between 2005 and 2014, the number of IE hospitalizations in persons with Opioid Use Disorder (OUD) increased by 122%, from 3,007 to 6,685, and then just 2 years later doubled to 13,125 cases in 2016 (Weiss 2020). In 2016, slightly more women (53%) than men (47%) with OUD were hospitalized for IE and >77% were younger than 49 years old; 83.3% were in a metropolitan location with 10% and 5.4% in a rural area adjacent to a city or a remote rural area, respectively. Over 54% relied on Medicaid insurance and 11.2% died during their hospital stay (Weiss 2020).

3. Rate of endocarditis in the United States and in West Virginia

There are no national or statewide data as IE and other serious bacterial and fungal infections are not reportable infections, and incidence is difficult to determine because "..criteria for diagnosis and the methods of reporting vary…" (Mandell, p. 991). However, multiple series indicate that there has been a dramatic increase in IE among PWID since 2000 (Keeshin 2016, Wurcel 2016, Weiss 2020). In addition, PWID have a high risk of recurrent IE. Data from a retrospective study from 2/07-3/16 showed that 212 of 390 total episodes occurred in PWID, 68 of whom (32%) had a second episode ($p<.001$), and 28/212 (12%) had additional recurrences beyond the second one (Rodger 2019). Misuse of peripherally inserted central catheters (PICC) used for intravenous antibiotic administration was associated with increased risk of recurrent IE ($p=.04$), which is why many hospitals will not discharge PWID with IE until the typical 6-week course of antibiotics has been completed. In this study, fungal IE was more common in second episodes than first episodes ($p=.004$) and was associated with higher mortality in second-episode IE with an adjusted odds ratio of 16.49 ($p=.041$), meaning it was more than 16.5 times common among PWID than non-drug users (Rodger 2019). Fungal IE is more difficult and more expensive to cure than bacterial IE, as the valvular lesions are larger and intravenous antifungals are costly. Another study comparing IE in PWID and non-drug showed that PWID were less likely to have a benign clinical course and had a higher frequency of septic complications (Chao 2004). A retrospective study from the Charleston Area Medical Center in West Virginia described 462 cases of IE among illicit drug users from 2006 to 2015, which represents more than a two-fold increase over that period. There was a significant increase in admissions with any type of drug use as well as associated IE. Increases in the category of "mixed drug use" strongly correlated with increased cases of IE during the study period ($p= 0.001$); "mixed drug use" strongly correlates with IV drug use but is not definitive. The geographic analysis based on admission home address zip code showed a pattern of clusters within the major population centers surrounding the southern coalfields. (Bates 2019).

4. Standard treatment for endocarditis

Typically, 6 weeks of intravenous bactericidal antibiotics (agents that kill the bacteria, not bacteriostatic agents that slow down bacterial growth) effective against the causative organism(s) are required; two such agents can sometimes be combined to produce rapid synergistic bacterial killing, which is more effective than either antibiotic alone. (Mandell) Fungal IE also typically requires 6 weeks of an intravenous antifungal agent. Left-sided disease may require management in an intensive care unit and surgical intervention; approximately 1/3 of patients with left-sided disease require surgery during the acute phase of infection for valve replacement or metastatic infection, which results in continued seeding of bacteria to other sites in the body from the valve ring or an adjacent structure (Mandell p. 1010). The hemodynamic status of the patient dictates whether cardiac surgery is needed and its timing. Left-sided IE complicated by congestive heart failure generally requires emergent surgery for survival. Non-emergent cardiac surgery may be required in persistent right-sided infection despite optimal antibiotic therapy if the cardiac valve(s) are sufficiently compromised. The 6-week duration of therapy is described as "typical" in cases where there are no additional complicating factors, such as liver or kidney

dysfunction, hemodynamic compromise, or other sites of infection such as an abscess in a visceral organ that need to be treated with antibiotics until it is resolved.

5. Standard Treatments for Other Infections Common with IDU

a. Osteomyelitis (bone infection). A bone biopsy or needle aspiration is performed to determine the causative bacterium; sometimes blood culture can also be used to identify the cause. Treatment is typically a combination of surgical debridement plus intravenous antibiotics, typically for at least 4 to 6 weeks.

b. Septic arthritis (joint infection). Joint drainage, either by aspiration, athroscopy or arthrotomy, is performed to determine the causative bacterium. In addition to drainage of pus from the enclosed joint space, treatment involves intravenous antibiotics, typically for 2 to 4 weeks.

c. Skin and soft tissue infections (SSTIs: cellulitis, abscess). It is difficult to recover a causative organism but almost all cases involve bacteria commonly found on the skin, such as Staphylococcal aureus, either methicillin-sensitive or methicillin-resistant (MRSA). Typically treatment involves 7-10 days of intravenous or oral antibiotics for cellulitis (skin infection), and incision and drainage for skin abscess plus 7-10 days of intravenous or oral antibiotics. Although this is the least serious IDU-associated infection, it is the most common, and therefore is the most common reason for hospitalization of PWID. In 2001, 0.07% of all non-federal facility hospitalizations were for SSTIs among PWID using heroin and cost over $193 million, with the rate of such hospitalizations doubling between 2001 and 2010, concentrated among PWID 20-40 years old (Ciccarone 2016).

d. Deep tissue abscess (brain, other organs). Identification of the causative organism via drainage of pus from the enclosed site is typically by performed by Interventional Radiology, although brain abscesses require neurosurgical drainage, plus intravenous antibiotics typically for a period of 6-8 weeks. The duration of treatment may be longer depending on radiologic evidence that abscess is resolved by CT or MRI scan.

F. Harm Reduction

1. What is “Harm Reduction”?

Harm reduction is a non-judgmental, non-coercive public health approach to minimize the harm from undesirable behaviors such as injection drug use, by minimizing morbidity and mortality. It does not condone these undesirable behaviors.

Harm reduction encompasses the provision of services and resources to people who use drugs and the communities in which they live to assist them in reducing the attendant harms of drug use. This is accomplished through community-based syringe services programs (SSPs, previously called needle or syringe exchanges) and overdose education and naloxone distribution (OEND) programs; often, SSPs include on-site OEND. These programs provide: sterile syringes and clean injection supplies (cookers cottons, alcohol swabs, sterile water); referrals for treatment of OUD; education about safer injection practices; education about safer sex practices and male and female condoms; testing for injection drug use-associated infections such as HIV and hepatitis C; vaccination for hepatitis A and B that can be fatal in a person who already has chronic hepatitis C; screening for sexually transmitted infections; abscess and wound care; and referrals for infectious diseases, transactional sex other medical services, and behavioral/mental health care (CDC SSP FAQs 2019).

2. Why Harm Reduction is Crucial for Individual and Community Health in the Opioid Epidemic

As noted above, the services provided by harm reduction programs that include syringe services can reduce the transmission of HIV (by ~50% per multiple studies); viral hepatitis A/B/C through a combination of safer injection practices, sterile syringes, clean injection supplies, and vaccination; sexually transmitted infections acquired from routine sexual behaviors as well as transactional sex (trading sex for drugs, money or other inducements); and prevention of opioid overdoses and overdose fatalities. The key element of syringe services programs is the development of trust between the clients and staff so that when a client is ready for drug treatment and other healthcare services, s/he will seek this referral from a trusted source. Despite the negative image of SSPs portrayed in public media, multiple studies have shown a range of benefits. SSPs decrease injection drug use and increase the number of clients entering recovery: PWID who use an SSP more likely to enter treatment for substance use disorder and stop injecting than those who do not use an SSP (Wodak 2006, Hagan 2000, Strathdee 1999, Bluthenthal 2001) and are nearly three times as likely to report a reduction in injection frequency as those who have never used an SSP (Hagan 2000). Importantly, new SSP clients are five times more likely to enter drug treatment as those who do not use SSPs (Hagan 2000). SSPs decrease HIV transmission (Gibson 2001, Des Jarlais 2005), decrease HBV (Hagan 1995) and HCV transmission (Hagan 1995, Des Jarlais 2005). Drug injection can also lead to bacterial and fungal infections and other complications. By providing access to sterile syringes and other injection equipment, SSPs not only help prevent transmission of bloodborne viral infections, they can also reduce the risk of other serious, life-threatening, and costly infections, such as endocarditis (heart valve infection), visceral (deep tissue) and brain abscesses, and serious skin infections; SSP-provided health care can provide early and easily accessible treatment to PWID that are often reluctant to seek care at an emergency room or other location (Grau 2002, Pollack 2002, Robinowitz 2014).

SSPs do not cause or increase crime (Marx 2000, Galea 2001). SSPs reduce the presence of needles in the community that can be a danger to first responders and other community members (de Montigny 2010, Doherty 2000, Tookes 2011). The existence of SSPs does not induce individuals naïve to injection drug use to begin injecting (Institute of Medicine 2006). Moreover, SSPs are highly cost-effective by preventing serious life-threatening infections, linking PWID to drug treatment programs, preventing overdose and the long-term neurologic damage that occurs in some cases where reversal is not timely enough. A couple of examples include the estimated over $450,000 lifetime cost of treating HIV (Farnham 2013) and the over $700 million annual cost of hospitalizations for drug-related infections (Ronan 2016).

Putting naloxone, the opioid overdose antidote, in the hands of community members—especially PWID—is the most effective way to prevent fatalities. Data from the City of Huntington show that in 2017, almost equal numbers of lives were saved by naloxone administration by the Community Naloxone Program as by Emergency Medical Services (M. Kilkenny, MD).

3. Standard Best Practices for Harm Reduction/Syringe Services

Best practices for harm reduction/syringe services programs require that they be managed according to evidence-based data, without pressure from elected officials and others local government officials to do otherwise.

Standard best practices for harm reduction/syringe services include: 1) providing the number of syringes that the individual states a need for instead of 1-for-1 exchange as this significantly reduces the time that a syringe circulates in the community; 2) providing clean injection supplies used to prepare drug for injection such as cookers, cottons, tourniquets, rinse water, alcohol swabs for cleaning the injection site—hepatitis C can persist on inanimate surfaces such as cookers so that even if individuals use their own syringes if they share these other materials they can still transmit and acquire hepatitis C; 3) offering testing for chronic viral infections, such as rapid on-site testing for HIV and HCV or blood draws for laboratory-based testing for these infections plus HBV for which there is no rapid test; 4) providing overdose education and naloxone distribution (OEND); 5) providing male and female condoms to reduce the transmission and acquisition of sexually transmitted infections; 6) educating clients about safer injection practices and safer sex practices; 7) providing referrals to substance use disorder programs, medical care including infectious diseases, and mental health care; 8) providing referrals to social services including food, shelter, childcare, educational and job training programs; 9) providing fentanyl test strips so that PWID can make informed decisions about how to use drug that may be part or entirely fentanyl or a fentanyl analogue. Best practices have been summarized by the American Foundation for AIDS Research (AmFAR 2013) and the national Harm Reduction Coalition https://harmreduction.org/syringe-access/syringe-access-tools/guide-to-developing-and-managing-syringe-access-programs/).

4. State of Harm Reduction and Related Initiatives in West Virginia and Cabell County

The Department of Health and Human Resources' Bureau for Public Health *Harm Reduction Program Guidelines and Certification Procedure* (revised August 27, 2018) outlines the minimum requirements for programs to receive DHHR funding. Certification is not required but ensures that programs follow the state's core guidelines (oeps.wvgov/documents/about/wv_hrp). Based on my recollection as a member of the Executive Committee of the Harm Reduction Coalition of West Virginia, as of the end of 2019, there were 18 syringe services programs in West Virginia, 16 located in county health departments and two in non-profit clinics. Local governments have closed two programs, including the state's largest SSP in Charleston that served over 6,000 clients.

The CHHD syringe services program, located at the health department, opened in September 2015. It is state-certified and operates on a "one for one plus" model, which means there is some flexibility in the one-for-one basis for the number of sterile syringes distributed in exchange for used ones that are returned. This is a change from the original model that was needs-based (distributing the number of sterile syringes needed regardless of the number returned); the change followed the closure of the Charleston Kanawha Health Department's program in March 2018 that also operated on a needs-based model. Another significant change in April 2018 was to alter the intake process to limit services to residents of Cabell County and City of Huntington. "Clients are now required to show proof of residency and residency is confirmed through the same process as the Division of Motor Vehicles and in conjunction with the Coalition for the Homeless." As a result, in 2019 there was a 50% decrease from 2018 in the number of new clients and the total number of PWID served by the program (CHHD Annual Report FY2019).

Other harm reduction services at CHHD include: HIV/HBV/HCV/STD testing; Hep A/Hep B vaccines; on-site recovery coach; condoms; family planning; wound care; linkage to behavioral health, social and medical services; naloxone and naloxone training; and prevention education literature. Naloxone training classes are offered one day a week and one evening each month. "With support from DHHR, the Cabell-Huntington Harm Reduction Program (CHHRP) began in September 2015 in response to surveillance indicators and community concerns regarding opioid overdose, overdose

deaths, HBV, HCV, and neonatal abstinence syndrome (NAS, infants born in opioid withdrawal due to maternal opioid use). When services began, 15 clients were seen in a two-hour clinic session and demand quickly grew. In 2016, CHHRP served 1,980 clients, dispensed 300,049 syringes, and collected 232,067 syringes." (https://oeps.wv.gov/harm_reduction/documents/training/hrp_white_paper.pdf).

The distribution of sterile syringes and clean injection material; testing for HIV, viral hepatitis and STDs; vaccinations; wound care; and referral to evaluation and treatment for infectious diseases are all important interventions for IDU-associated infectious diseases and their impact on community health.

5. Barriers to Best Practices in Harm Reduction in West Virginia

There are multiple barriers to best practices in the state. (1) The stigma of OUD, as well as the stigma of medication assisted treatment (MAT) that relies on the use of methadone, buprenorphine (whether coformulated with naloxone or not), or naltrexone plus psychosocial counseling. Despite the fact that MAT has an extensive evidence base for efficacy and safety, there is a persistent mistaken belief that it is "just another drug for a drug". Methadone and buprenorphine have been shown to help those with OUD achieve and maintain recovery, save lives from overdose, and improve response to treatment for HIV and HCV. Stigma has influenced the attitude of residents and elected officials to harm reduction programs and has resulted in the closure of two in the past two years. Other important barriers are (2) significant state underfunding to the county health departments that house the majority of the SSPs that results in limited access to SSP services—some SSPs are only open a few hours each month. The lack of funding affects staffing and significantly affects the purchase of (3) sterile syringes that cannot be purchased with federal funds, such as block grants to states from the Substance Abuse and Mental Health Services Administration (SAMHSA) by law, and (4) expensive rapid test kits for HIV and HCV used on-site that yield results in 10-15 minutes.

G. Recommendations and Opportunities for Improving Outcomes of Infectious Diseases Caused by Opioid Use Disorder (OUD)

For the past five years I have been conducting federally- and state-funded research in the infectious and other medical complications of injection opioid use, primarily in southern West Virginia. My experience working with county health departments, regional comprehensive behavioral health agencies, first responders, the county drug court system, local government, community organizations, PWID, as a member of the Executive Committee of the Harm Reduction Coalition of West Virginia, as the Chair of the national HIV Medicine Association (part of the Infectious Diseases Society of America), and as an infectious diseases specialist provides the background to the recommendations offered below. Having participated in both the "Integrating Responses at the Intersection of Opioid Use Disorder and Infectious Disease Epidemics" sponsored by the National Academies of Sciences, Engineering and Medicine in March 2018 and Association of Schools and Programs of Public Health Task Force on Public Health Initiatives to Address the Opioid Crisis in 2018-2019, many of my recommendations described below will also reflect the outcomes of those proceedings.

1. Importance of Integration/Co-location of Services for OUD and Infectious Diseases

Infectious diseases (ID) specialists are often the first physicians to see a patient with OUD through an encounter for the diagnosis and treatment of an injection drug use-associated infection, either in the hospital or in the outpatient setting. As a result, ID physicians have increasingly taken on the additional role of providing medication-assisted treatment to their patients. Ideally, integration, or at least co-location of OUD and ID treatment, makes sense because of the chronic nature of these

diseases. This can work bidirectionally: ID physicians can obtain a waiver to prescribe and manage buprenorphine along with management of the infection, and MAT programs can engage ID specialists to care for their chronically infected patients on-site. MAT and ID care have also been successfully integrated within primary care settings as described in our review **"**Integrated models of care for individuals with opioid use disorder: how do we prevent HIV and HCV?" (Rich 2018). In fact, integration can go beyond care for OUD and infectious diseases to also include on-site mental health services. Integrated/co-located care is crucially important in rural settings where access to specialty care for OUD and infectious diseases is limited or non-existent, especially in federally qualified health centers (FQHCs). This has been recognized by the Health Resources and Services Administration (HRSA) and the Substance Abuse and Mental Health Services Administration (SAMHSA) through their joint pilot project "…focused on building understanding among providers on how to best implement MAT to increase adoption of medications in the treatment of substance use disorders in primary care, substance use, and community mental health programs." (https://bphc.hrsa.gov/qualityimprovement/clinicalquality/substance-use-disorder-primary-care-integration). Infectious diseases and primary care providers can be incentivized to provide MAT to their patients and addiction psychiatrists can be incentivized to integrate screening for chronic infectious diseases and STDs into OUD management. Taking it a step further, in general shortages of ID-trained specialists, addiction psychiatrists and rural primary care providers can be addressed through loan forgiveness and other incentives.

Integration can take other forms from successful MAT initiation in the Emergency Department for patients presenting with problems that are manageable on an outpatient basis (D'Onofrio 2015) to active support for opioid withdrawal and MAT initiation during hospitalization for serious acute infection such as endocarditis (Fanucchi 2016). The COVID-19 pandemic has demonstrated the utility of telemedicine support from specialists and primary care providers. Continued insurance reimbursement for telemedicine can make a significant difference in access to needed care, especially in rural areas.

2. Education and Training of Primary Care Providers (PCPs)

PCPs can successfully manage the chronic viral infection associated with injection drug use through educational and experiential distance learning programs. The first and best-known is Project ECHO (Extension for Community Healthcare Outcomes), a collaborative model of medical education and across New Medico (Arora 2007). In early 2020, a model represented by the West Virginia Hepatitis Academic Mentoring Partnership (WVHAMP) combines in-person didactics with distance learning to empower rural PCPs to screen, diagnose, evaluate, treat and cure chronic hepatitis. WVHAMP is structured to permit PCPs to meet West Virginia Medicaid's requirement that HCV treatment be provided with oversight from a specialist: a hepatologist, gastroenterologist, or infectious diseases physician. The program emphasizes how to introduce the goal of curative treatment to patients with OUD and to collaborate with MAT providers (J. Feinberg, MD, founder).

3. Prevention Opportunities

Both harm reduction/syringe services programs and primary care providers have an important role in the prevention of the infectious and medical sequelae of injection drug use. These include: 1) vaccination for hepatitis A & B, and human papillomavirus (HPV); 2) routine interval screening for HIV, hepatitis B & C according to national guidelines; 3) safer sex education and access to male and female condoms; 4) access to long-acting reversible, contraception (LARC) for women; 5) HIV pre-exposure prophylaxis (PrEP) that currently depends on consistent use of oral medications, but Food and Drug Administration approval of long-acting injectable PrEP is anticipated later this year; 6) widespread

overdose education and naloxone distribution programs aimed at family members, community members, first responders including volunteer fire departments in rural areas, and people who use drugs; 7) ready availability of naloxone in schools, performance spaces, bus terminals, sports arenas and willing commercial entities like the program in Charleston where businesses with naloxone available have a decal affixed to the store window or door—in other words, in public spaces where defibrillators are commonly seen.

4. Expansion of OUD Treatment and Support Services and Interventions

Peer Recovery Support Specialists (PRSS) are individuals with OUD in long-term recovery that receive state certification after completing a standard curriculum, field supervision and passing a test. PRSS can offer support to PWID without stigma and provide assistance with needed services including active linkage to drug treatment programs, medical and mental health care and facilitate access to social services. Moreover, PRSS offer full-time employment to persons in long-term recovery who may be disqualified from other jobs because of prior legal problems. PRSS can provide assistance at county health departments, SSPs, schools and community organizations; can provide information to schools, religious groups, and other community organizations and agencies. Their presence in the community can be important both as role models to persons with OUD and as a force to defuse stigma. Becoming a PRSS can be a stepping-stone to further education and advancement to a career as a addiction counselor. However, current salaries for PRSS in West Virginia are low (often requiring additional support such as food stamps), so enhanced salaries are required.

5. Specialized Treatment for Endocarditis Outside of the Hospital

Development and expansion of facilities that could manage both OUD treatment and continued intravenous antibiotics would likely result in fewer patients leaving the hospital against medical advice before their course of treatment is completed and would be cost-effective compared to a six-week stay in the hospital. The Center for Hope and Healing affiliated with WVU Medicine in Morgantown is a model for such an approach. Another approach is the Endocarditis program at Ruby (Garret Cooper)

6. Strategies to Overcome Barriers

It goes without saying that treatment for OUD and the infectious complications of IDU would not be possible for most West Virginians without continuation of the Affordable Care Act. Our research in southern West Virginia (not yet published) demonstrates that stigma and lack of access to transportation are the most significant obstacles for treatment, whether for OUD or infectious diseases. Overcoming stigma will require substantial public reconsideration of how we treat PWID—the HIV epidemic is forty years old and people living with HIV are still subjected to stigma although there has been some improvement over time. Funding for public and social media campaigns are needed to start the conversation about disparaging persons with the disease of OUD. Innovative pilot programs to evaluate how an affordable, rural transportation-on-demand system—a rural Uber-lookalike—might work.

In summary, the opioid epidemic has done tremendous damage to West Virginia and to the City of Huntington and Cabell County in particular. There are specific needs for the prevention of the infectious complications of drug use and for screening, diagnosing, evaluating, and treating (curing or managing) these life-threatening infections, not only for the benefit of the affected individuals and their families, but also for the public health of the greater community. These are needs that must be met in a humane society.

I reserve the right to amend or supplement my opinions in this matter considering any new or additional information.

Pursuant to 28 U.S.C. § 1746, I declare under penalty of perjury that the foregoing is true and correct.

Dated: August 3, 2020

JUDITH FEINBERG, MD

Attachments:

- CV
- List reliance materials